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10/539,208	05/24/2006	David Raab	B&B-135-US	2327

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EXAMINER	
ZHOU, SHUBO	

ART UNIT	PAPER NUMBER
1631	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/539,208	RAAB ET AL.	
	Examiner	Art Unit	
	SHUBO (Joe) ZHOU	1631	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *3/30/10, 12/11/09*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-30* is/are pending in the application.

4a) Of the above claim(s) *17-30* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-16* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *12/12/07*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Election/Amendments/Status of the Claims

Applicant's response filed 3/30/10 is acknowledged. It's hereby clarified that there was no sequence election requirement for Group I in the restriction requirement mailed 11/12/09.

Applicants' election of Group I (claims 1-16) in the response filed 12/11/09 is acknowledged. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)).

The amendment filed 12/11/09 is acknowledged and entered.

Claims 1-30 are pending.

Claims 17-30 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected invention, there being no allowable generic or linking claim. Election was made **without** traverse in the reply filed on 12/11/09.

Claims 1-16 are under examination.

Sequence Rules Compliance

This application contains sequence disclosures that are encompassed by the definitions for nucleotide and/or amino acid sequences set forth in 37 CFR 1.821(a)(1) and (a)(2). Such sequences are present on pages 41, 43, 46, 53, etc. of the specification. However, this application fails to comply with the requirements of 37 CFR 1.821 through 1.825 because the sequences are not followed by a sequence identifier (SEQ ID

NO:X). It should be pointed out that while the sequence (AASeq1) is deemed fictional in the specification, it is still encompassed by the definitions for nucleotide and/or amino acid sequences set forth in 37 CFR 1.821(a)(1) and (a)(2), and thus should be listed on the Sequence Listing and be in compliance with all the requirements of 37 CFR 1.821 through 1.825. Applicants are given the same response time regarding this failure to comply as that set forth to respond to this office action. Failure to comply with these requirements may result in ABANDONMENT of the application under 37 CFR 1.821(g). Applicants are reminded that it is required that SEQ ID Nos be amended into the specification at each sequence, and that when a sequence is presented in a drawing regardless of the format or the manner of presentation of that sequence in the drawing, the sequence must still be included in the Sequence Listing and the sequence identifier ("SEQ ID NO:X") must be used, either in the drawing or in the Brief Description of the Drawings.

Specification

The specification is objected to because of the following including informalities:

The following guidelines illustrate the preferred layout for the specification of a utility application. These guidelines are suggested for the applicant's use.

Arrangement of the Specification

As provided in 37 CFR 1.77(b), the specification of a utility application should include the following sections in order. Each of the lettered items should appear in upper case, without underlining or bold type, as a section heading. If no text follows the section heading, the phrase "Not Applicable" should follow the section heading:

(a) TITLE OF THE INVENTION.
(b) CROSS-REFERENCE TO RELATED APPLICATIONS.
(c) STATEMENT REGARDING FEDERALLY SPONSORED RESEARCH OR DEVELOPMENT.

(d) THE NAMES OF THE PARTIES TO A JOINT RESEARCH AGREEMENT.
(e) INCORPORATION-BY-REFERENCE OF MATERIAL SUBMITTED ON A COMPACT DISC.
(f) BACKGROUND OF THE INVENTION.
(1) Field of the Invention.
(2) Description of Related Art including information disclosed under 37 CFR 1.97 and 1.98.
(g) BRIEF SUMMARY OF THE INVENTION.
(h) BRIEF DESCRIPTION OF THE SEVERAL VIEWS OF THE DRAWING(S).
(i) DETAILED DESCRIPTION OF THE INVENTION.
(j) CLAIM OR CLAIMS (commencing on a separate sheet).
(k) ABSTRACT OF THE DISCLOSURE (commencing on a separate sheet).
(l) SEQUENCE LISTING (See MPEP § 2424 and 37 CFR 1.821-1.825. A "Sequence Listing" is required on paper if the application discloses a nucleotide or amino acid sequence as defined in 37 CFR 1.821(a) and if the required "Sequence Listing" is not submitted as an electronic document on compact disc).

In the instant case, there are no section headings for any section in the specification.

Trademarks are used in this application, such as GENBANK™ on page 56. All trademarks should be capitalized wherever they appear and be accompanied by the generic terminology. Although the use of trademarks is permissible in patent applications, the proprietary nature of the marks should be respected and every effort should be made to prevent their use in any manner that might adversely affect their validity as trademarks.

The disclosure is objected to also because it contains an embedded hyperlink and/or other form or browser-executable code. Such code is present in the specification at least on pages 53, 56. Applicants are required to delete the embedded hyperlink and/or other form of browser-executable code. See MPEP ' 608.01.

Claim Rejections - 35 USC § 101

35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

Claims 1-10 and 14-15 are rejected under 35 U.S.C. 101 because the claimed invention is directed to non-statutory subject matter.

This rejection is based on the court's decision in *In re Bilski*, and on the Office's recent "Interim Examination Instructions for Evaluating Subject Matter Eligibility Under 35 USC 101," effective August 24, 2009, which is available at the Office's website at http://www.uspto.gov/web/offices/pac/dapp/opla/2009-08-25_interim_101_instructions.pdf.

The instant claims are drawn to a method for optimizing a nucleotide sequence for the expression of a protein on the basis of the amino acid sequence of the protein, which comprises the following steps of

- generation of a first test sequence of n codons which correspond to n consecutive amino acids in the protein sequence, where n is a natural number and is less than or equal to N, the number of amino acids in the protein sequence;
- specification of m optimization positions in the test sequence which correspond to the position of m codons at which the occupation by a codon, relative to the test sequence, is to be optimized, where m is smaller than or equal to n and m<N;

- generation of one or more further test sequences from the first test sequence by replacing at one or more of the m optimization positions a codon of the first test sequence by another codon which expresses the same amino acid;
- assessment of each of the test sequences with a quality function and ascertaining the test sequence which is optimal in relation to the quality function;
- specification of p codons of the optimal test sequence which are located at one of the m optimization positions, as result codons which form the codons of the optimized nucleotide sequence at the positions which corresponds to the position of said p codons in the test sequence, where p is a natural number and p is smaller than or equal to m iteration of the preceding steps, where in each iteration step the test sequence comprises the appropriate result codon at the positions which correspond to positions of specified result codons in the optimized nucleotide sequence, and the optimization positions are different from positions of result codons.

As set forth in the Interim Examination Instructions (pages 4-5), a process claim, to be statutory under 35 USC 101, must pass the machine-or-transformation test (M-or-T test), that is, a claimed process must:

(1) be tied to a particular machine or apparatus; or

(2) particularly transform a particular article to a different state or thing.

In the instant case, the claimed process is not tied to a particular machine or a particular apparatus. Furthermore, there is no physical transformation recited and achieved by the claimed process as it merely manipulates data.

The rejection could be overcome by amendment of the claims to be tied to a particular machine or to recite and achieve a physical transformation by the method steps. Applicant, however, is cautioned against introducing new matter into the claims.

Applicant is also reminded that the court has pointed out that the involvement of the particular machine/apparatus or transformation in a claimed process must not merely be an insignificant extra-solution activity. See Flook, 437 U.S. at 590. Preambles, data-gathering and/or outputting result steps may fall within the category of such insignificant extra-solution activity.

As to claims 14 and 15, which are drawn to a "computer program," comprising program codes which can be executed by a computer, a computer program, per se, i.e. the software, without being on a computer readable medium is nonstatutory. See MPEP 2106 IV (B) (1).

As to claim 16, which is drawn to a computer readable medium comprising a computer program, while the instant specification does not explicitly define the scope of the limitation of "computer readable medium," one skilled in the art would understand that computer readable medium includes carrier wave, which is a signal. For example, Fiekowsky et al., in US patent 6,090,555 (Date of Patent: July 18, 2000), define computer readable medium as being "a CD-ROM, floppy disk, tape, flash memory, system memory, hard drive, and a data signal embodied in a carrier wave." See column 14, claim

12. Bornstein et al., in US patent 6,1443,88 (Date of patent : Nov. 7, 2000) state, "The computer readable medium of the present invention generally includes a tape, a floppy disk, a CD ROM, a carrier wave. In a preferred embodiment, however, the computer readable medium of the present invention is a carrier wave." See column 8, lines 33-37.

Therefore, at least one embodiment of the instant claim is drawn to carrier wave or a signal encoded thereon a computer program.

It was held by the court that claims that recite nothing but the physical characteristics of a form of energy, such as a frequency, voltage, or the strength of a magnetic field, define energy or magnetism, per se, and as such, are nonstatutory natural phenomena. O'Reilly, 56 U.S. (15 How.) at 112-14. Moreover, it does not appear that a claim reciting a signal encoded with functional descriptive material, e.g. a computer program, falls within any of the categories of patentable subject matter set forth in § 101.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.

2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1-16 are rejected under 35 U.S.C. 103(a) as being unpatentable over Hoover et al. (IDS document filed 12/12/07, Nucleic Acids Research, 2002, Vol. 30, No. 10 e43).

For the record, a search of the website of Nucleic Acids Research (NAR) reveals that Hoover et al. was published in May 2002. See attached copy of NAR's web pages (printed from http://nar.oxfordjournals.org/archive/2002.dtl on 6/21/10)

As set forth above, the instant claims are drawn to a method for optimizing a nucleotide sequence for the expression of a protein on the basis of the amino acid sequence of the protein, which comprises the following steps (step numbers were added by the examiner for convenience):

1) generation of a first test sequence of n codons which correspond to n consecutive amino acids in the protein sequence, where n is a natural number and is less than or equal to N, the number of amino acids in the protein sequence;

2) specification of m optimization positions in the test sequence which correspond to the position of m codons at which the occupation by a codon, relative to the test sequence, is to be optimized, where m is smaller than or equal to n and m<N;

3) generation of one or more further test sequences from the first test sequence by replacing at one or more of the m optimization positions a codon of the first test sequence by another codon which expresses the same amino acid;

4) assessment of each of the test sequences with a quality function and ascertaining the test sequence which is optimal in relation to the quality function;

5) specification of p codons of the optimal test sequence which are located at one of the m optimization positions, as result codons which form the codons of the optimized nucleotide sequence at the positions which corresponds to the position of said p codons in the test sequence, where p is a natural number and p is smaller than or equal to m iteration of the preceding steps, where in each iteration step the test sequence comprises the appropriate result codon at the positions which correspond to positions of specified result codons in the optimized nucleotide sequence, and the optimization positions are different from positions of result codons.

Hoover et al. disclose a method and system for automated designing oligonucleotides based on the amino acid sequence of a protein/peptide. The method

includes optimizing the nucleotide sequences based on codon usage, melting temperature, etc. See at least the Abstract. The method includes reverse translate the inputted protein sequence into a first test sequence comprising codons which correspond to the consecutive amino acids in the protein sequence, where the number of codons is equal to the number of amino acids in the protein sequence. See page 2 of 7 and Fig. 1. This reads on step 1) of the instant claim 1. While Hoover et al. do not use any symbols to represent the number of codons, it would be readily apparent to one skilled in the art that any character or symbol could be used for such a purpose. For the sake of convenience for discussion in this Office action, n is used for the number of codons, and N for the number of amino acids in the test sequence. This test sequence is then broken into odd number of contiguous sections of smaller test sequences, each with a plurality of specified codons at positions corresponding to the positions of the amino acids of the test sequence for optimization. Hoover et al. disclose that stochastic optimization is used, and codons of the sections are swapped with other codons. Hoover et al. stress that during each optimization step, the number of mutations as well as changes in sizes diminish as the optimization process progresses. Hoover et al. also disclose that quality functions are used to assess the quality the test sequence and sections thereof including calculating scores based on codon frequency, hairpin formation and deviations from the desired melting temperature (involving GC content) and size, etc., and at the end of each optimization step, the score is recalculated for each section. When no further improvements of the scores, the sequences are optimized, and each an optimized codon is specified for each position. See Fig. 1 and page 3 of 7. This reads on steps 2)-5) of the instant claim 1. Again, it would be readily apparent to one skilled in the art that any

character or symbol could be used for representing the number of codons in each section. For the sake of convenience for discussion in this Office action, m is used for the number of codons in each section. Clearly, m is small than n or N above as m represents sections of N.

Again, while Hoover et al. do not use particular characters, e.g. n, N, m, etc. to represent the number of codons, amino acids, etc., it would have been obvious to one of ordinary skill in the art at the time of the invention that any characters or symbols would have been used and sufficient for representations. Furthermore, since these characters would be used for representing the number of amino acids, codons, etc., in the test sequence or sections thereof, it would be obvious that they are natural numbers.

Hoover et al. also disclose a device, system and computer program for the method. See pages 3 of 7 and 4 of 7.

Conclusion

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Shubo (Joe) Zhou, whose telephone number is 571-272-0724. The examiner can normally be reached Monday-Friday from 9 A.M. to 5 P.M. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Marjorie Moran, can be reached on 571-272-0720. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Patent applicants with problems or questions regarding electronic images that can be viewed in the Patent Application Information Retrieval system (PAIR) can now contact the USPTO's Patent Electronic Business Center (Patent EBC) for assistance. Representatives are available to answer your questions daily from 6 am to midnight (EST). The toll free number is (866) 217-9197. When calling please have your application serial or patent number, the type of document you are having an image problem with, the number of pages and the specific nature of the problem. The Patent Electronic Business Center will notify applicants of the resolution of the problem within

5-7 business days. Applicants can also check PAIR to confirm that the problem has been corrected. The USPTO's Patent Electronic Business Center is a complete service center supporting all patent business on the Internet. The USPTO's PAIR system provides Internet-based access to patent application status and history information. It also enables applicants to view the scanned images of their own application file folder(s) as well as general patent information available to the public. For all other customer support, please call the USPTO Call Center (UCC) at 800-786-9199.

/Shubo (Joe) Zhou/

SHUBO (JOE) ZHOU, PH.D.

PRIMARY EXAMINER